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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/778,187	02/06/2001	Peter Robert Baum	2873-US	9057
22932	7590	06/11/2004	EXAMINER	
IMMUNEX CORPORATION LAW DEPARTMENT 1201 AMGEN COURT WEST SEATTLE, WA 98119			HADDAD, MAHER M	
			ART UNIT	PAPER NUMBER
			1644	

DATE MAILED: 06/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/778,187	Applicant(s) BAUM ET AL.	
	Examiner Maher M. Haddad	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 April 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 18-63 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 18-63 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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RESPONSE TO APPLICANT'S AMENDMENT

1. The examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Maher Haddad, Art Unit 1644, Technology Center 1600.

2. Applicant's amendment, filed 4/7/04, is acknowledged.

3. Claims 18-63 are pending and under Examination in the instant application.

4. In view of the amendment filed on 4/7/04, only the following rejections are remained.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 35-36 and 46-54 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 35, 36 and 46-54 are ambiguous in reciting hybridizing under conditions of "moderate stringency" (claims 35 and 46-54) or "severe stringency" (claim 36). There does not appear to be a definition in the specification as filed that clearly provides the metes and bounds of these conditions. Thus it is unclear which conditions are actually claimed.

Applicant submits in the Response filed 4/7/04 that the stringency conditions, as stated in the specification, are defined in Sambrook et al, and that the moderate or severe hybridization condition was known in the art at the time of filing. Further, Applicant argues in conjunction with case law that the claims be read in light of the specification, reasonably apprise those skilled in the art and are as precise as the subject matter permits.

However, the temperature and salt concentrations at which the hybridization is performed has a direct effect upon the results that are obtained. The hybridization results are directly related to the number of degrees below the Tm of DNA at which the experiment is performed. The specification fails to provide the metes and bounds of such conditions.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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8. Claims 18-63 stand rejected under 35 U.S.C. 112, first paragraph, for the same reasons set forth in the previous Office Action mailed 8/1/03.

Applicant's arguments, filed 4/7/04, have been fully considered, but have not been found convincing.

Applicant argues regarding Mertz et al teachings that a single amino acid changes can alter or abolish the ability of CTLA to interact with CD80 and CD86 that Not any amino acid changes would affect the protein binding. Applicant submits that about 50% of the single amino acid changes did not abolish the binding. Further, Applicant submits that Mertz et al data is not surprising because the data show that only the mutations that occur in the conserved surface patch on the A'GFCC' face abolish binding to CD80 and/or CD86, while the other mutations, which occur on the BED surface, did not. Applicant submits that such data are not shown to demonstrate that any single amino acid changes would affect the binding activity of CTLA-4.

Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Due to the large quantity of experimentation necessary to obtain "variance of SEQ ID NO: 2 or SEQ ID NO: 4", to generate the infinite number of derivatives recited in the claims (for at least 80% of SEQ ID NO:2 would be 88²⁰ variants), and to determine the specific activity of the infinite variants, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to the same, the complex nature of the invention, the state of the prior art which establishes that biological activity cannot be predicted based on structural similarity, and the breadth of the claims which embrace a broad class of structural variants, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope. The contribution of mutations at different amino acids to the function of the polypeptide is highly heterogeneous. Thus, Mertz et al reference demonstrated that event a single amino acid substitution will often dramatically affect the biological activity and characteristic of a protein. Thus it is unpredictable if any functional activity will be shared by two polypeptides having less than 100% identity over the full length of their sequences.

Applicant submits that the examiner fails to provide as to why a variant with 95% identity is enabled but not are those with at least 80% or at least 90% identity. The applicants wish to remind the examiner that the claims are drawn to an isolated polypeptide that is not only based on sequence identity or with a mutation, but also on its capability of binding to LDCAM and/nr B7L-1.

Applicant argument is acknowledged, however, the recitation "at least 80% or 90%" encompasses a broader scope of variation which requires more evidence in order to satisfy the statute. Applicant has not provided any objective evidence to support the at least 80% or 90% identity variants claimed.

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9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e1) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

35 U.S.C. § 102(e), as revised by the AIPA and H.R. 2215, applies to all qualifying references, except when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. For such patents, the prior art date is determined under 35 U.S.C. § 102(e) as it existed prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. § 102(e)).

10. Claims 8-63 stand rejected under 35 U.S.C. 102(e) as being anticipated by Baker et al. (US 2002/0198147), as evidenced by the attached alignments for the same reasons set forth in the previous Office Action mailed 8/1/03.

Applicant's arguments, filed 4/7/04, have been fully considered, but have not been found convincing.

Applicant submits that the Examiner has erred in concluding that Baker et al anticipates the instant claims because Baker et al does not claim all the subject matter that are instantly claimed by the applicants. Applicant submits that referenced SEQ ID NO: 61 is not the same as that in the instant SEQ ID NO: 2 or 4. Specifically, Applicant points that SEQ ID NO: 61 is not the same as SEQ ID NO: 2 because the former is devoid of two amino acid residues that occur in the latter. SEQ ID NO: 61 is not the same as SEQ ID NO: 4 because, when aligned to each other, SEQ ID NO: 61 differs from SEQ ID NO: 4 in one amino acid (i.e. Phe31Leu). Applicant request a clarify the description that SEQ ID NO: 61 differs from SEQ ID NO: 4 by the two amino acid deletion and the additional amino acid in the C-terminus.

Contrary to Applicant assertion Baker et al anticipates the claimed invention. The two amino acids difference ($440/442 = 99.5\%$) between claimed and referenced polypeptide are within the claimed at least 90% or 80%. Furthermore, instant claims recited a full and partial amino acid sequence of SEQ ID NO: 2 or 4 (with a signal peptide or without a signal peptide, i.e., 1-374, 1-442, 39-374 or 39-442). The referenced polypeptide of SEQ ID NO: 61 comprise an amino acid sequence that is 100% identical to either 39-373 or 39-442 of claimed SEQ ID NO: 2. Regarding Applicant request for clarification regarding the difference between referenced SEQ ID NO: 61 and claimed SEQ ID NO: 4. Referenced SEQ ID NO: 61 differs from claimed SEQ ID NO: 4 by two amino acid deletions at positions 6 and 7, five amino acid substitutions at position Leu15Phe, Lys166Thr, Phe245Ileu, Thr350Ser and Gly352Arg. Such substitutions read on the threshold of at least 80% identical amino acid sequence of SEQ ID NO: 4. Furthermore, the term "comprising" in instant claims is open-ended. It would open up the claims to include the 440 amino acid sequence.

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Applicant further argue that Baker et al there are six claims drawn in Baker et al., claims 12-17. Except claim 14, which does not recite the ATCC deposit for PRO355, these claims are drawn to a polypeptide which is least 80% identical or has a score of at least 80% positives to the full length SEQ ID NO: 61 or full length PRO355 protein, or to a chimeric molecule comprising any of these polypeptides. Applicant contends that nowhere in the claim set does Baker et al recite a polypeptide which is as recited in the instant claims.

Contrary to Applicant assertions Baker et al claims the claimed invention for example published claim 12 recites at least 80% amino acid sequence identity to an amino acid sequence of SEQ ID NO:61. For example claim 12 recites: An isolated polypeptide having at least 80% amino acid sequence identity to an amino acid sequence shown in FIG. 24 (SEQ ID NO:61. Claim 13 recites: An isolated polypeptide scoring at least 80% positives when compared to an amino acid sequence shown in FIG. 24 (SEQ ID NO:61), claim 14 recites: An isolated polypeptide having at least 80% amino acid sequence identity to an amino acid sequence encoded by the full-length coding sequence of the DNA deposited under ATCC accession number 209529.

11. No claim is allowed.

12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be

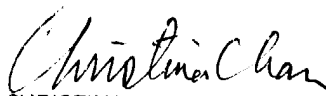
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obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maher Haddad, Ph.D.

Patent Examiner

June 10, 2004


CHRISTINA CHAN
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